Figure 2

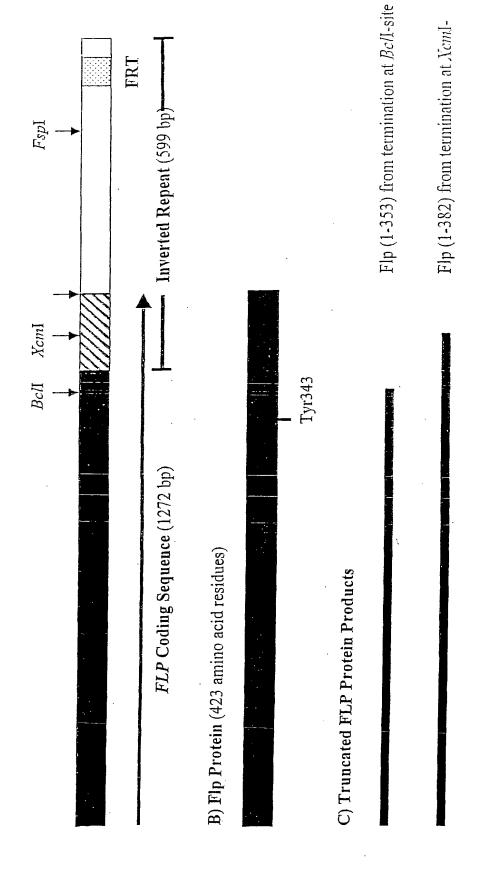
AmpR. Eagl FLP.E. Ybal Anal IR. 11037 bps Norl Eag J 011 REP2 Eco RI Xcm I HindIII Fsp1Aval_ Eco RU, Hin all Hpal_ Psil

 $Eco\, {
m II}$ REP 1 PstI IR2 Hpal2-micron Cla I, Eco RI 6318 bps FLP STB AvaI ori SnaBI IR1 REP2 Eagl ApaI1/63

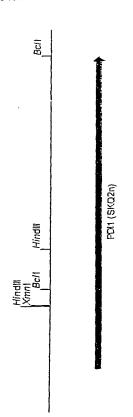
Figure 1

Figure 3

A) Restriction Endonuclease Sites used for DNA Insertions in FLP and the FLP Inverted



igure 4



 F_{sp1} F_{sp2}

\Nde l Bc/I Hin dIII

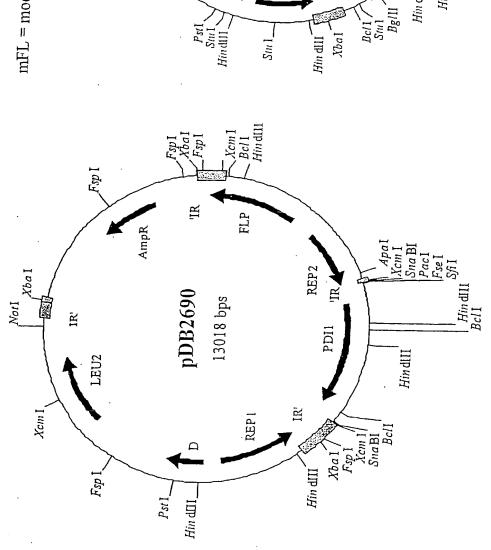
Sphi

Sfil Fsel Pac I Apa I

Figure 7

Figure 6

mFL = modified HSA(pre)/MF α 1(pro) fusion leader sequence



mADHIt IR'

16292 bps

REP 1

Modified T

PRBIp , mFL AmpR '

FLP

TR REP2

Hin d I I I / Bc I I I / Hin d I I I I

PDII

Stul

Figure 8

mFL = modified HSA(pre)/MF $\alpha I(pro)$ fusion leader sequence

mHSA-pre = modified HSA-pre leader sequence

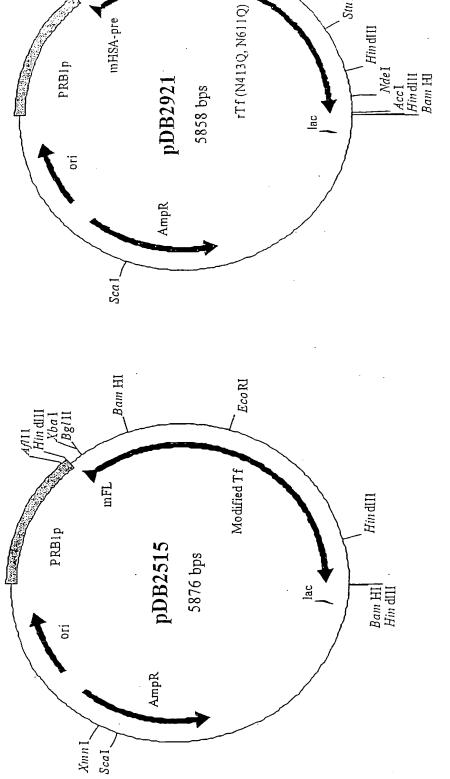
Figure 9

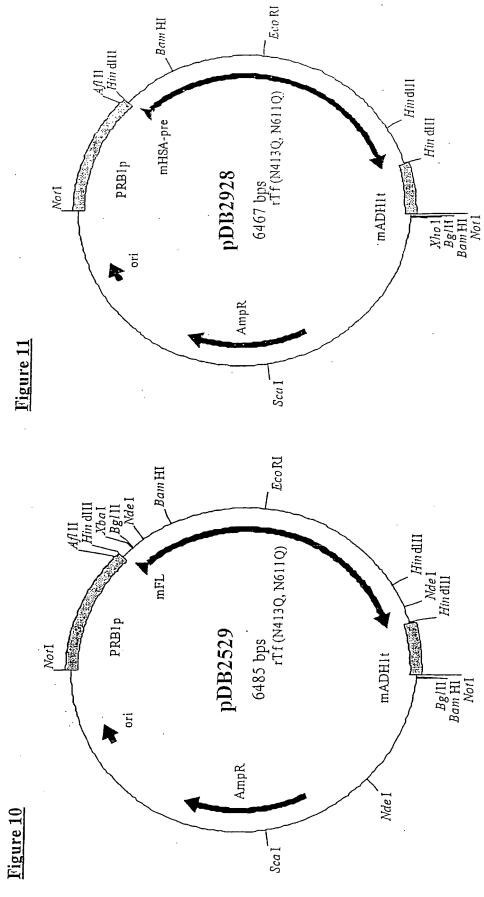
Bam HI

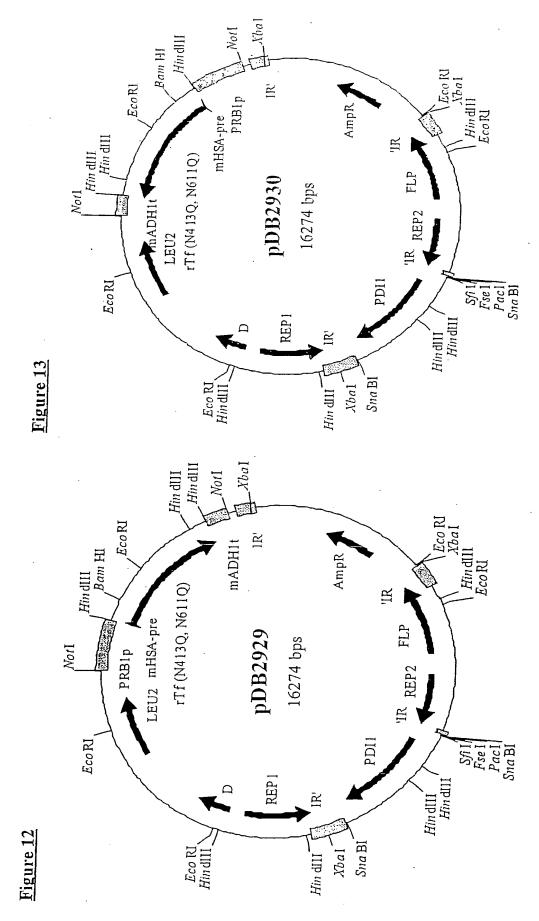
mHSA-pre

Nde I Hin d111

Eco R







7/63

-Xha I Hin dill Bam HI Eco RI mHSA-pre PRB1p II. ,Not1 ,Hin dl II Hin dl II AmpR rTf (N413Q, N611Q) | Hindiil EcoRl 14293 bps mADH1t LEU2 Eco RI REP 1 ĭ XbaIHim dIII Eco RI Hin di II Hin dlll Hin dIII Xbal Eco RI IR mADH1t BamHI Hin dIII AmpR rTf (N413Q, N611Q) Hin dIIIPRB1p / LEU2 mHSA-pre 14293 bps Norl Eco RI REP1 XbaI Hin dIII Eco RI HindII

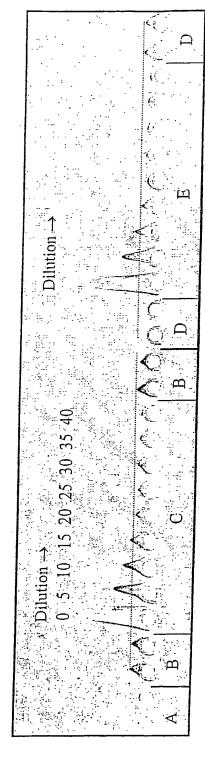
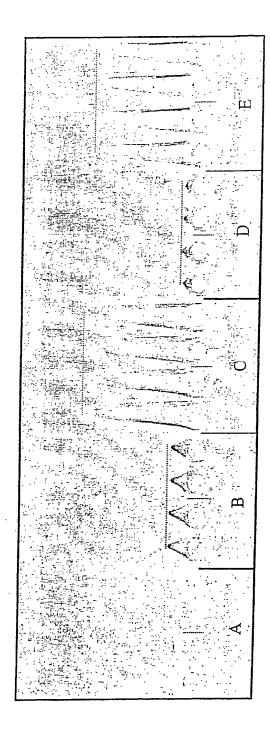
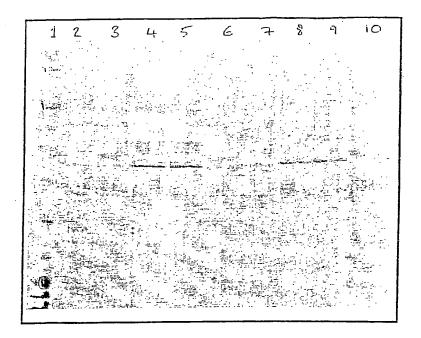


Figure 16



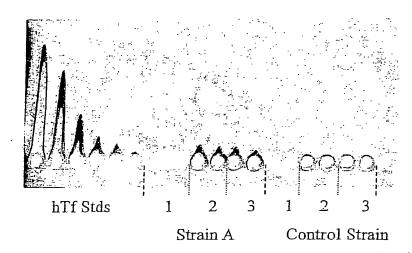
igure 17

Figure 18



5

Figure 19



12/63

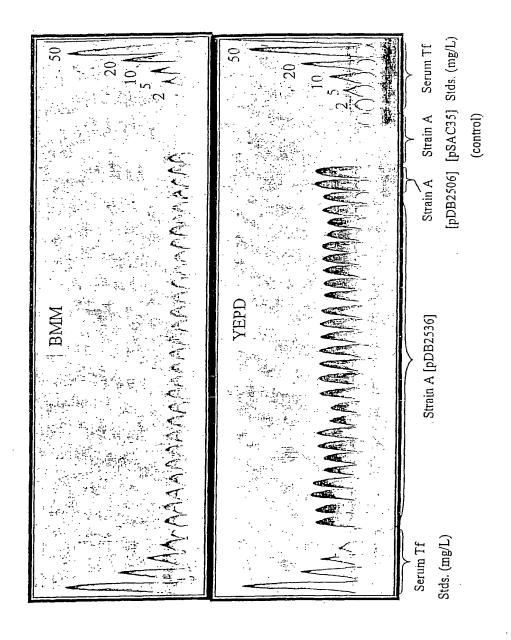


Figure 20

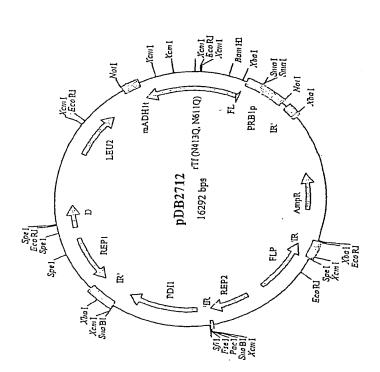
WO 2005/061718

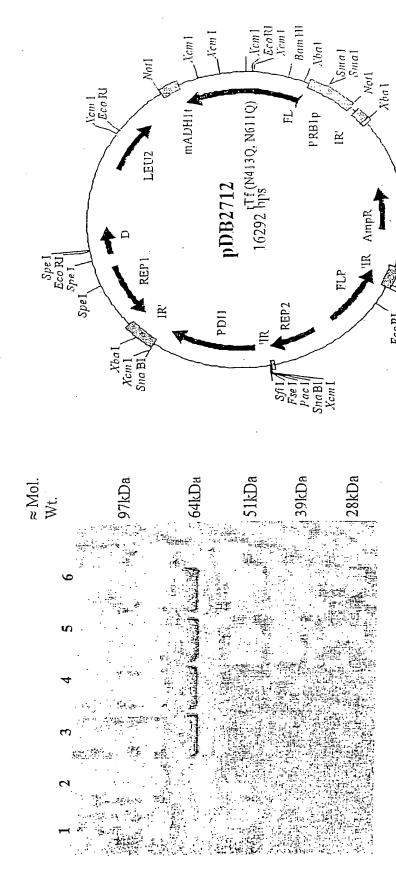
Figure 21

		1 2 3 4	. 5	≈ Mol. Wt.
5	·			191kD
10				97kDa
10				64kDa
				51kDa
15				

14/63







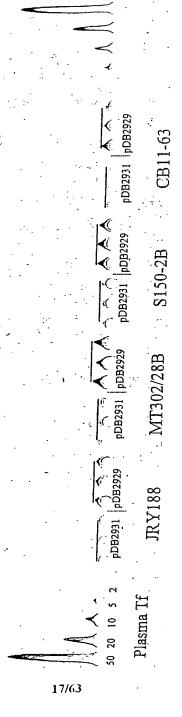


Figure 26

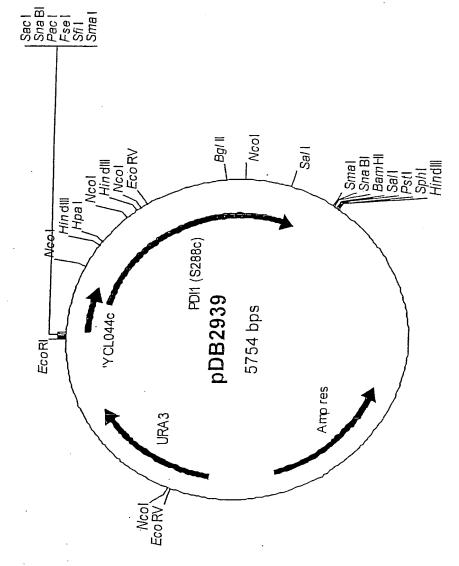


Figure 27

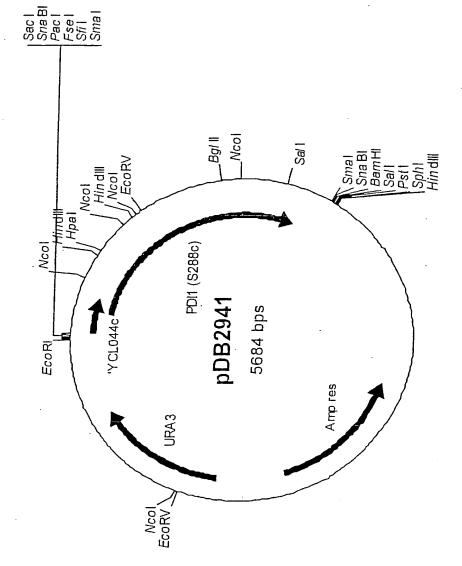
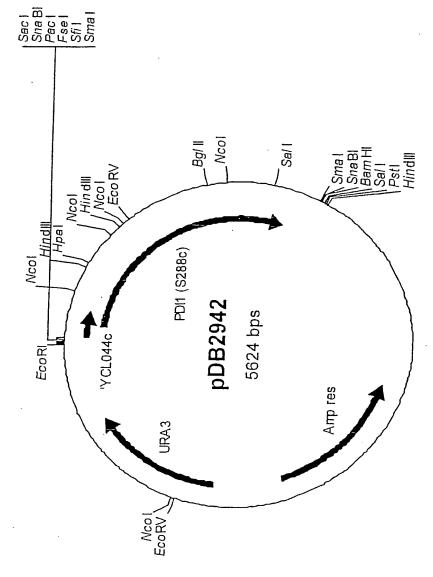
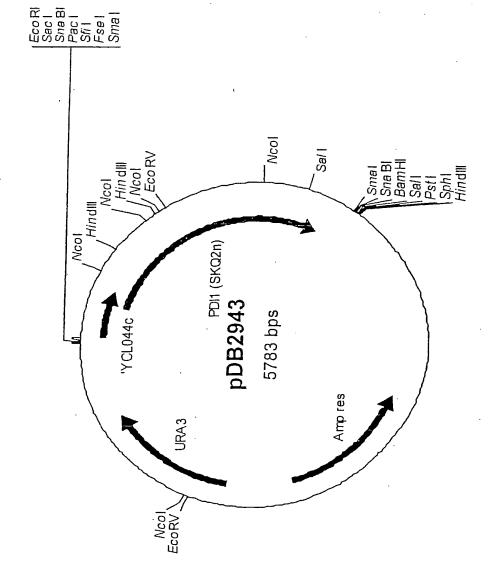


Figure 28







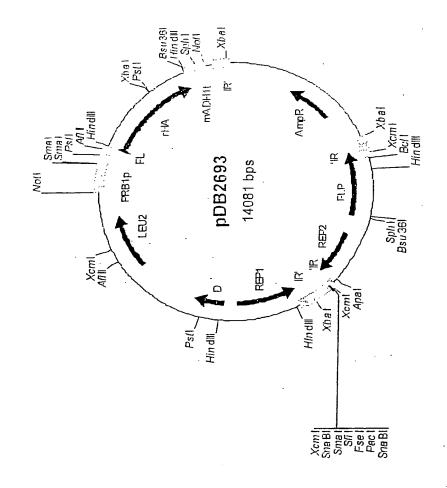
igure 30

Figure 32

BamHII Pst | Sal I | Sna BII | Soh I | Sna II | Hindill | Nool | DB2945

Hindill | 5649 bps | Any res | Sna II | Fae II | Nool | EcoRY | Nool | Nool | EcoRY | Nool | Noo

Figure 31



Scall Mae!

AmpR 6203 bps

THA

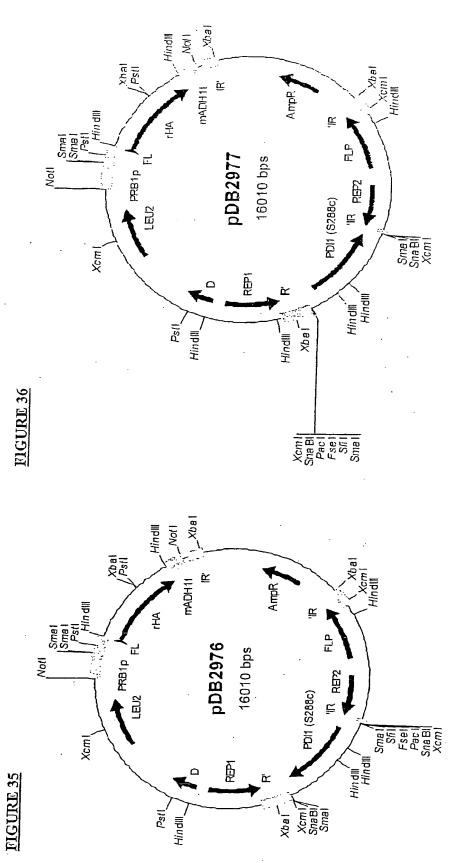
Nae!

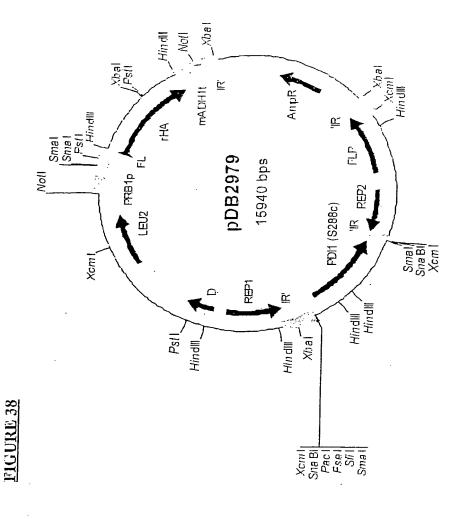
AmpR 6203 bps

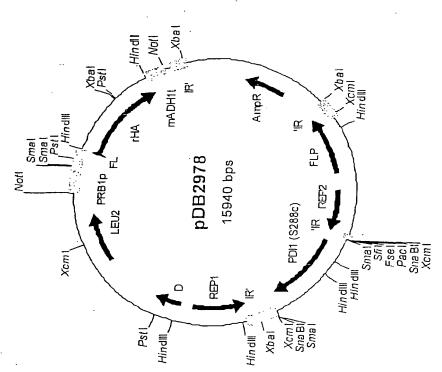
THA

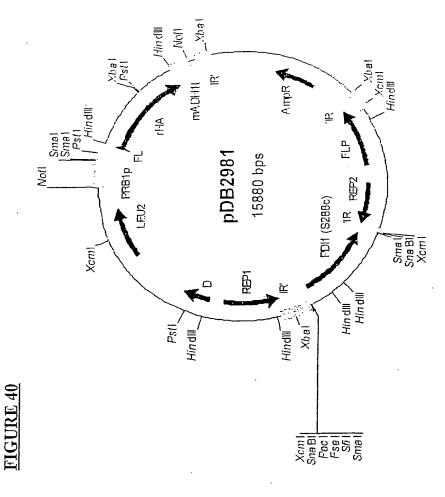
Nou!

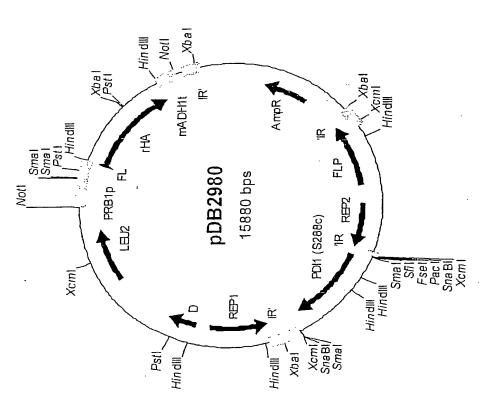
No











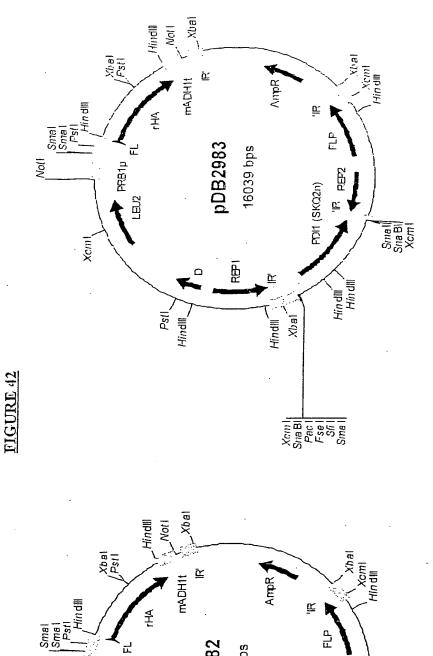


FIGURE 41

Not!
Sma!
Sma!
Sma!
FL
Hind!!!

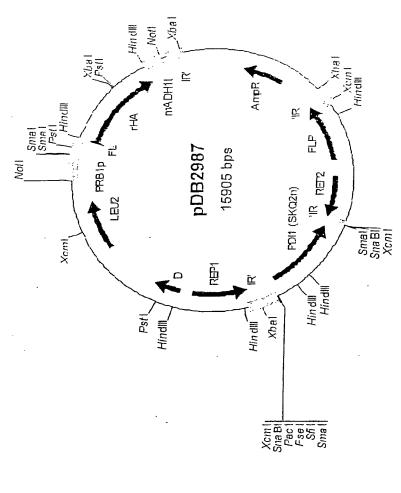
Pst!

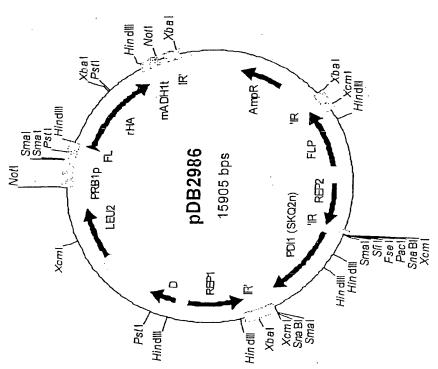
Xba!

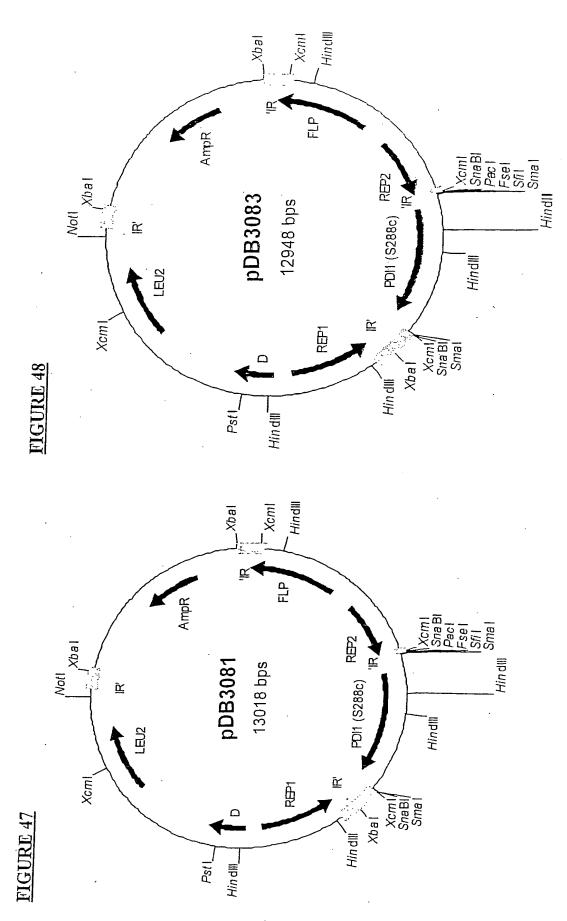
Xba!
Xba!
Xcm!
FL
Hind!!!
Sma!
Sma!
Sma!
FL
Hind!!!
Sma!
Sma!
Sma!
FLP
Hind!!!
Sma!
Sma!
Sma!
FLP
Sma!
FLP
Sma!
FLP
Sma!
Sma!
Sma!
FLP
Sma!
Sma!
FLP
Sma!
FLP
Sma!
FLP
Sma!
FLP
Xba!
FLP
Xcm!
Fac!
Sma!
FLP
Xcm!
Fac!
Sma!
Fac!
Fuc Manual
Fac!
Fac.

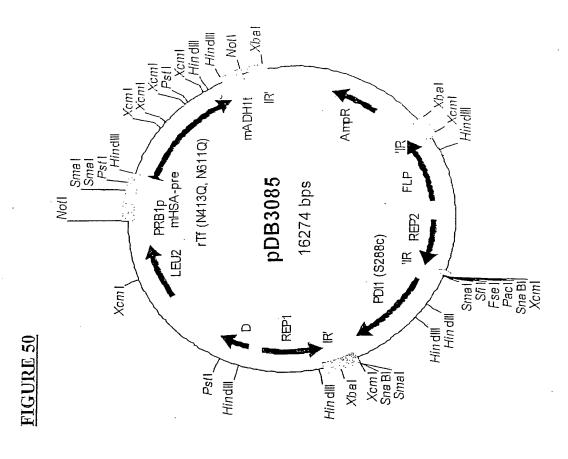
Ē mA DH1t FRB1p FL pDB2985 15969 bps Nof FDII (SKQ2n) Small Sna Bl Xcm I Xcm H H Hindill Hindill Pst Hud Hin dill FIGURE 44 Xcml Sna Bl Pac I Fse I Sn I

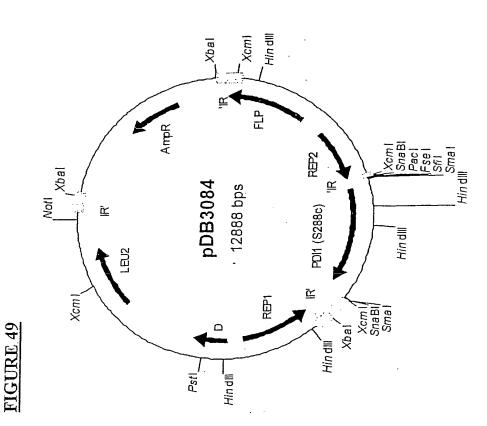
Hindill Small Smal

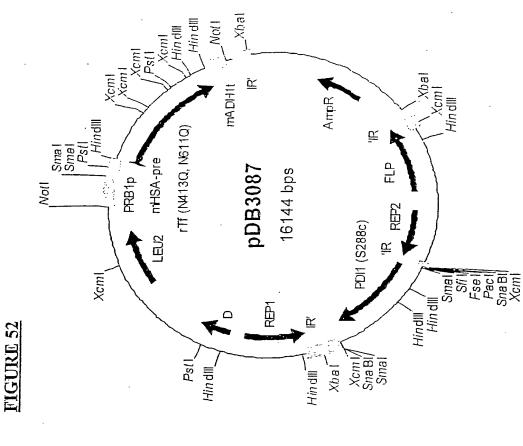








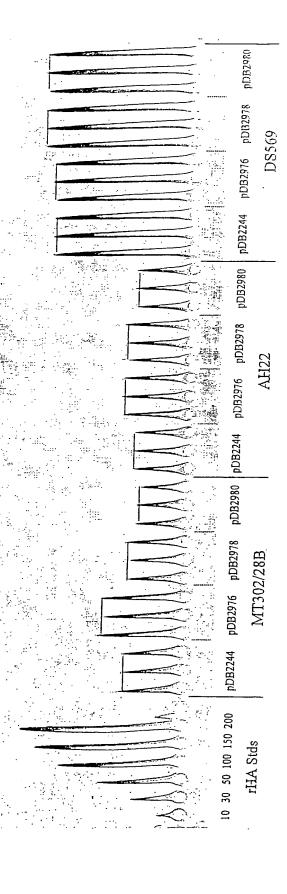


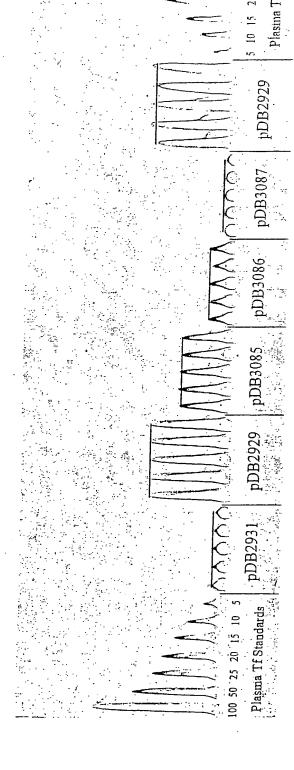


mADH1t AmpR • rTf (N413Q, N611Q) Ē mHSA-pre pDB3086 16204 bps PRB1p Notl REP2 PDI1 (S288c) Small Sfill Fsell Pacll SnaBll Xcml Xcm HindIII / 页 Xcm1/ SnaBl/ Sma1 Pstl Xba. HindIII Hin dill

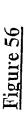
32/63







IGURI



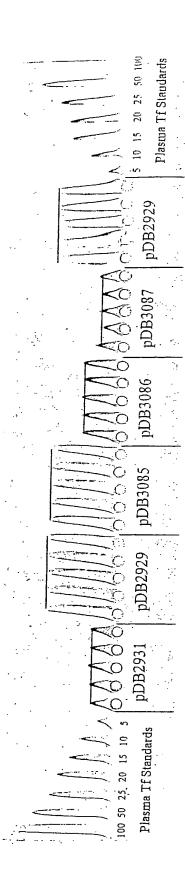
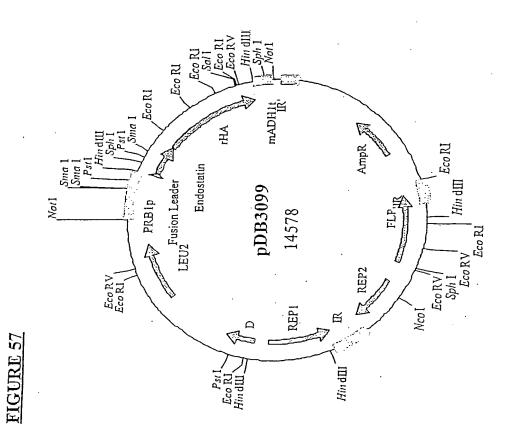
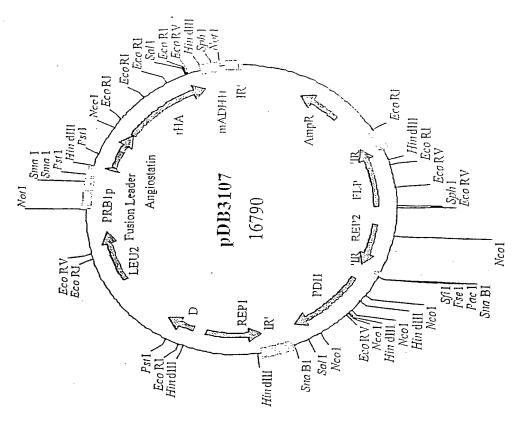


FIGURE 58

| Nort | Sma 1 | Path ettil | Sma 1 | Eco R1 |







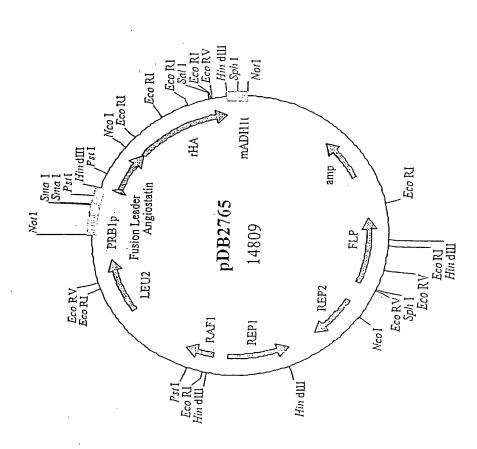
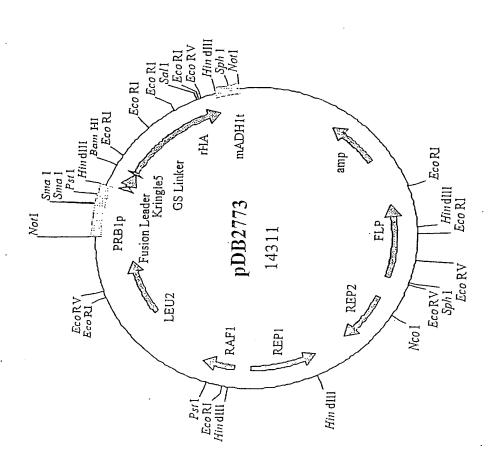
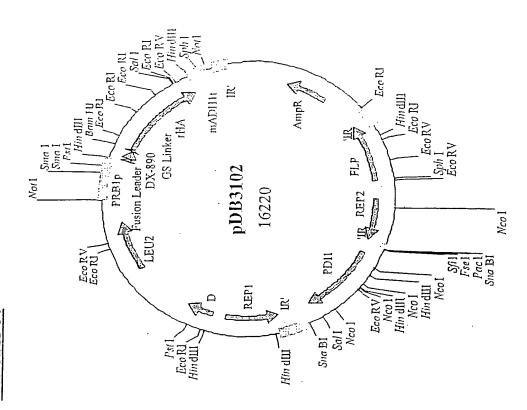
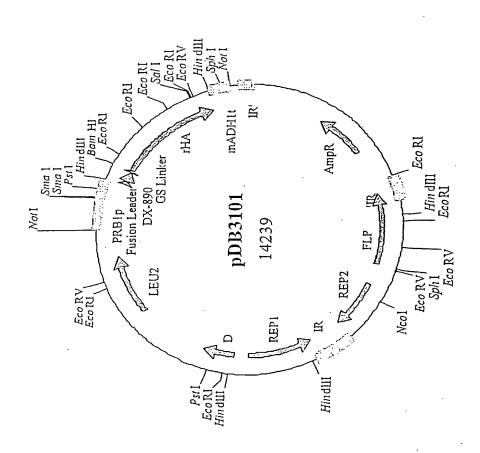


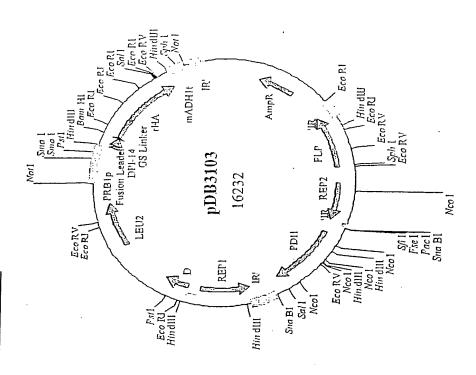
FIGURE 62

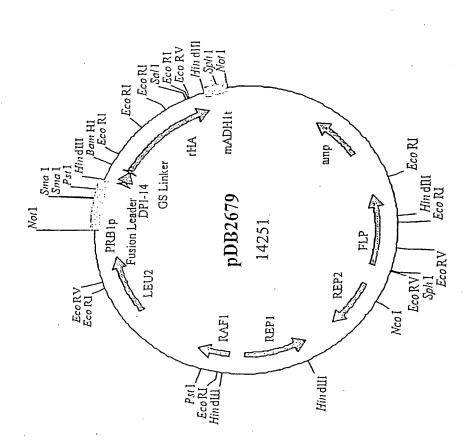
된 AmpR 🞢 , 'Hin dill Eco Ri Eco RV mADHIt No/1 16292 IR REP2 Nco I LEU2 Eco RI, PDII Sfil Fsel Pac I Sna Bi Nco 1 |
Nco 1 |
Hin dill |
Nco 1 | Eco RV Nco I Sna Bl Sal 1 Hin dill

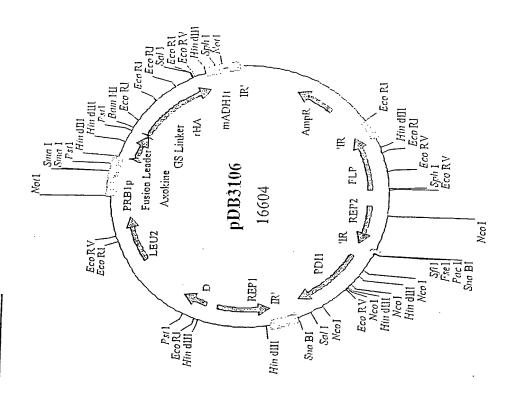












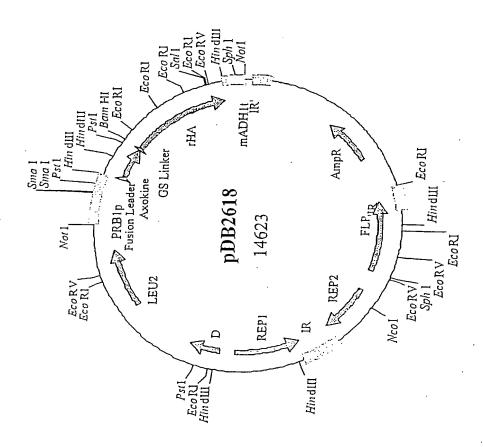
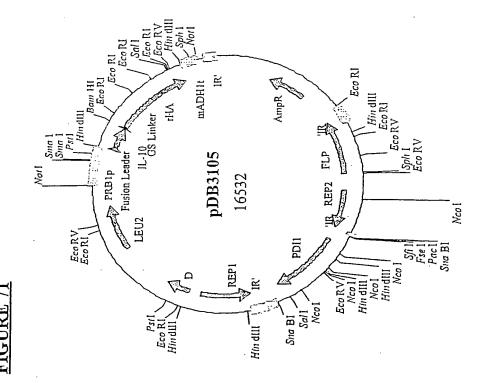


FIGURE 70

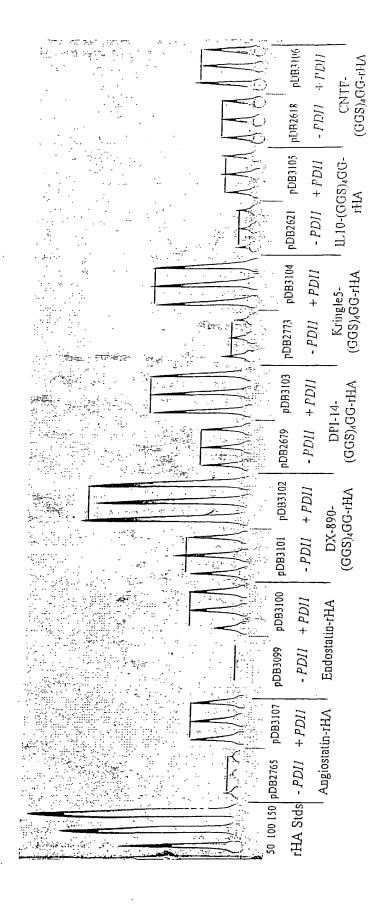
FIGURE 69

From 1
Since 1
Since 1
Since 1
Since 1
Since 1
From 1
From

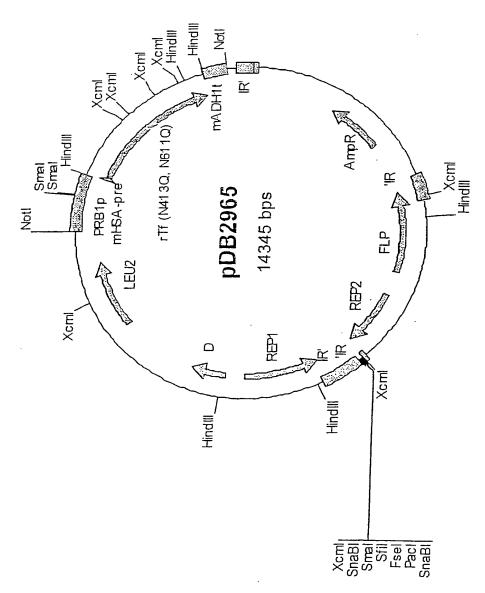
Bam HI Eco RI Eco RI Eco RI IL-10 GS Linker Smal Smal rHAFusion Leader Hin dII PRB1p 6715 bps Smal Not1 mADH1t Not I ori B



44/63



TGURE 72



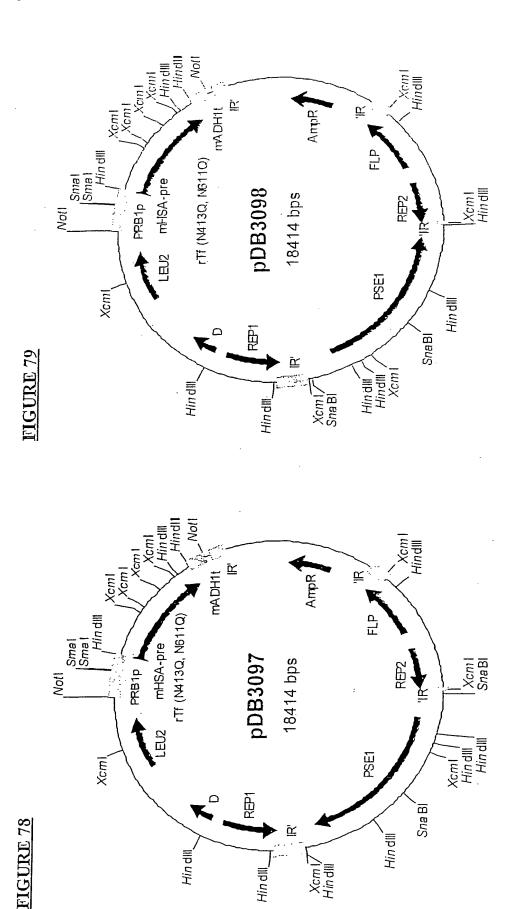
160

Scal Scal Small Small Small Scal amp "lacz" amp lacz" amp hindli snaBl Hindli Mdel Xmnl Hindli Mdel Xmnl Hindli SnaBl Hindli Shall Shall Shall Shall Hindli Mdel Xmnl Hindli SnaBl Hindli Hindli Hindli Hindli SnaBl

ĬΥ AmpR : pDB3090-pDB3093 rTf (N413Q, N611Q) mHSA-pre 15504 bps PRB1p 딥 No(I REPS ORMZ SnaBl Pac [SnaBl Xcm l Xcm Xcm1/ Sna Bl/ Smal/ Sfil/ Fsel/ Sna Bl HindIII Hin elli

FIGURE 75

FIGURE 77



50/63

Hin dIII_

Xcm I/ Hin dill

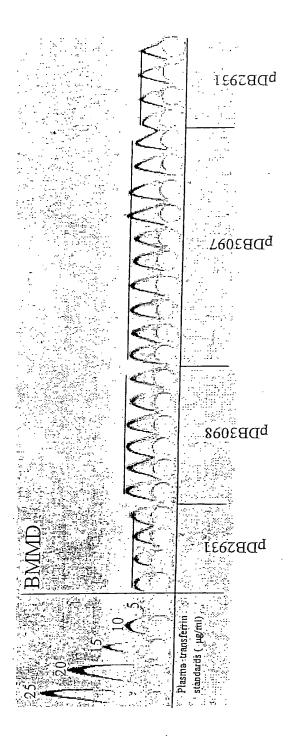
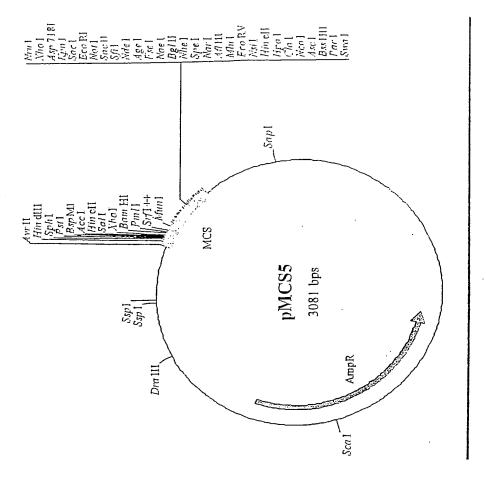


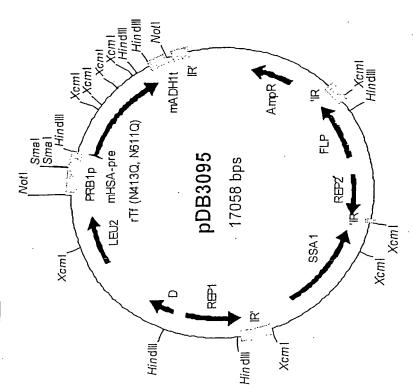
FIGURE 81

mADH1t 员 rTf (N413Q, N611Q) 딮 Smal Smal mHSA-pre pDB3094 PRB1p / 17058 bps Notl REP2 LEUZ Xcm Xcm $\underline{\underline{\sigma}}$ FIGURE 82 Xcm Hind Hind Xcm1

Bamel Sapl Small Sapl Hindli Sapl lacz' Sapl Eco Ri Small Bamel Hindli Sapl lacz' Pati Eco Ri Eco Ri Eco Ri Hindli Hindli

FIGURE 85





4	I
نة	
Ξ	
<u>:</u>	
	•

1.5 2025	a fransfeirin vrds (jg/ml)
v.ir.	Plashi standa
	DB293
	:
2	. acasaad
	bDB3095
	
	pDB3095
	F
\$ \$ £	v
	· ·
	ı <u>.</u>
	^b DB306 t
	:
	•
	:
7 [· ·
	DBS931
A. E	· ·
24	feirin g/ml)
	a trans rds (山
200	Plasma tran standards (1
	₽ ' <u>10</u>

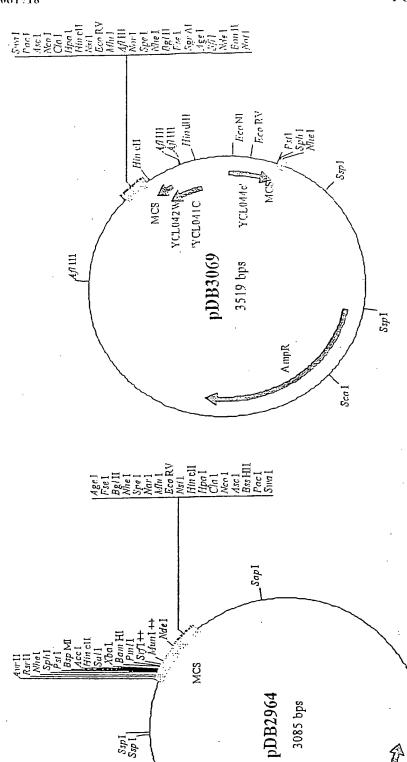
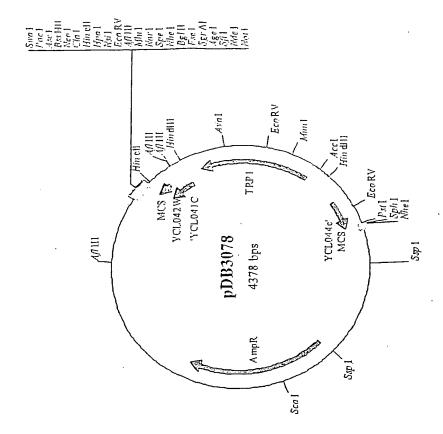


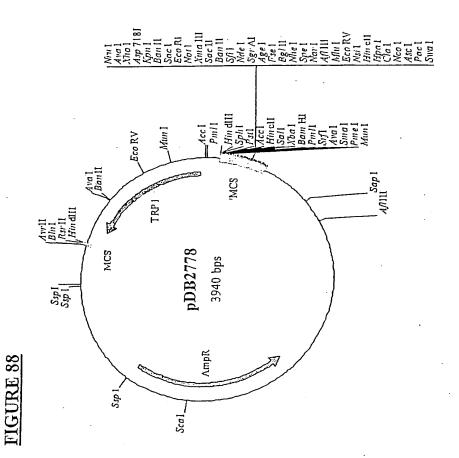
FIGURE 86

Ssp I

Dralli







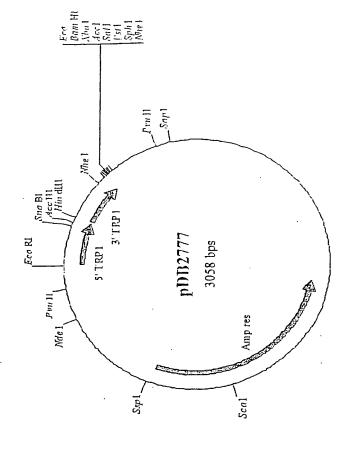


FIGURE 91

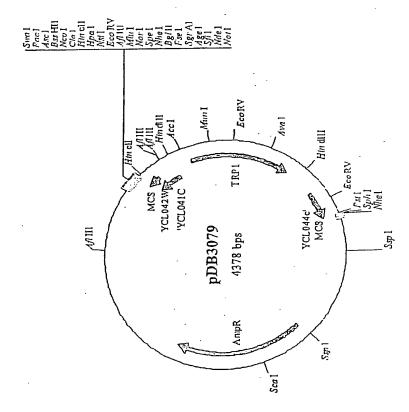
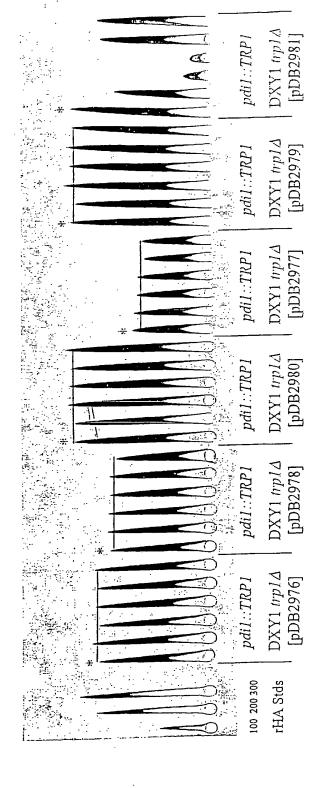


FIGURE 90



300-200-100 rFIA Stds

FIGURE 92

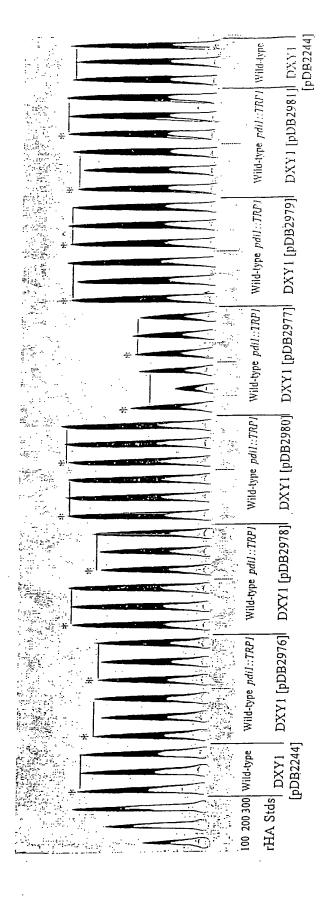


FIGURE 93

Figure 94A

- T	
Alignment Workspace of Ex 20 December 2004 15:04	kspace of Ext. meg D. Hein (Weighled) 804 15:04
Տշ89c long ՏԱՂշո long	CIPATCHILITITICAATTICAACAGIGIPACATTIGITIACAACACACAAAAACAAAAACAAAAAACAAAAACAAAAAA
S288c long SKQ2n long	TRIBUTIGITE COCIC CANTITICITICATE CARACTERIANI CANTITITA A COLOR CONTROLLA A CANTITICATE CANTITICATION CONTROLLA A CANTITICATICA A CANTITICATICA A CANTITICATICA A CANTITICATICA A CANTITICA A CANTITI
S288c long SKQ2n long	TITICIOCIOSTICCOGLICATORIO CONTROLO CON
S288c long SKQ2n long	CONCIDENTIONATOR TO A 16 3 TO 3 TO 3 TO 3 TO 40 4 TO 40 4 TO 410 4 TO 420 CONCIDENTIAN TO THE A 10 4 TO 44 TO CONCIDENTIAN TO A 10 4 TO 4 TO 4 TO CONCIDENTIAN TO A 10 4 TO 4 T
S288c long SKQ2n long	AGACTITIAGITGAGAAAAACATTACCTTGGCCAGATCGCTGTGCAGAATCGGGGGAAACAAAACAATCCAGGGTTCCCAAGGTTTGAAGATTTTCAAAAAAAA
S288c long SKQ2n long	AACASOGATIGITAACAAATUGATTAACAASOACTIAGAAGAACTIGOCTAATUGATOTAATUGAAGAAAAGACAAACUGAAGAAGAAGAAAAGAAAA

Figure 94B

Alignment Workspace of E 20 December 2004 15:04	späce of ExLimeg J. Hein (Weighted) Page 2 04 15:04
S288c long SKQ2n long	ACCAGETURE CENTRACE AND ACCOMPANIES OF A SECOND AND ACCOMPANIES OF A SECOND AC
S288c long SKQ2n long	ACGACTROGRESSION AND ACCACGACGACGACGACGACGACGACGACGACGACGACGA
S288c long SKQ2n long	AUCOCTICACOSTICATIVITADA A A A TODA TODA A CONTROCOMENTA A TODA TODA CONTROCOMENTA TO TODA TODA TODA TODA TODA TODA TODA
S288c long SKQ2n long	GSGITPACTIGITCTPACAAGAAGAAGAAGAAGAAGAAGAAGACTICTTTACCCAAGTIGGCCAAAAAAAAAA
S288c long SKQ2n long	GAABATICGGORGACACGOCGCAAACHIGAACAATICCCICTAITTICCAICCAACAACAANAAAACTICAAAATICGGORGACTICAAACTATICGGORGACTICAAAATICGGORGACTICAAAAATICGGORGACTICAAAATICGGORGACTICAAAATICGGORGACTICAAAATICGGORGACTICAACATICAAAATICGAAAATICGGORGACAATICGAAAATICGGORGACAATICGGORGACAATICCCICTICAAAATICGGAAATICGGORGACAATICGGORGAAATICCCICTICAATICAACAATICAAAATICGGAAAATICGGORGACAATICCCICTICAATICCCICTICAAAATICGGAAAATICGGAAAATICGGAAAATICGAAAATICGAAAATICCCICTAATICACACAATICCCICTICAAAATICGGAAAATICGGAAAATICGAAAATICGAAAATICGAAAATICCCICTAAAAATICCAACAACAACAACAAAAAAAA
S288c long SKQ2n long	CAGOCGITICA COARTICA COARTICA CONTRACA CIPAL COARTICA CA CACACACATICA COARTICA CARTICA COARTICA COARTI

Figure 94C

Alignment Workspace of Ex 20 December 2004 15:04	meg J. Heln (Weig
S288c long SKQ2n long	GATCTTCORPARACYCCTCTGTCCAATUGGTGGGGGGGGGGGGGGGGGGGGGGGG
S288c long SKQ2n long	GIGGICACIGIPAGAGANTIGGCCAAGATAGAGATAGAGATAGAGATAGAGACAGACAGA
S288c long SKQ2n long	ACAGOOSTICGIDARIOSTINACCOARCHATICGICTINA/ACCAGGIGGIDACCOARTICGITACCARGGITCAACATICGITGGACTICTITGACTICTITGACTICTITGACTICTITGACTICGACTICTITGACTICTITGACTICTITGACTICTITGACTICTITGACTICTITGACTICTITGACTICTITGACTICTITGACTICTITGACTICTICGACTICTICGACTICTICGACTICTICGACTICTICGACTICTICGACTICTICGACTICTICGACTICTICGACTICTICGACTICTICGACTICTICGACTICTICGACTICTICGACTICTICGACTICTICGACTICTICGACTICTICGACTICTACACTICTICGACTICTACACTICTACACTICTACACTICTACACTICACTICACTICACACTICTACACTICTACACTICTACACTICACTICACTICACTICACTICACTICTACACTICTACACTICTACACTICAC
S288c long SKQ2n long	CATCAASSAAACGSTCACTTCGAAGGSTRAAGSCTTTGTBACGSAAGCCCCAGGSAAAAACSTGAGSAAGCCGAAGCTTSACCCAAGCCGAAGCTLACTTG 1660 1670 1680 1750 1750 1700 1710 1710 1720 1730 1740 1750 1750 CATCAAGSAAAACGSTCAAGCTTCAAGSAAAACGSTCAAGCTTGAAGCTTGAAGCCTTGTAAGSAAAAAAAAAA
S288c long SKQ2n long	ACECICAAUTOSCICAACAAAAAGOCATICACAAUGAATIGIBACICAGITIGEITUITICATIRAADAAAANAADAAAAATITICAAGAAGITITIUT 1770 1780 1790 1860 1879 1870 1870 1870 1870 1870 1870 1840 1840 1850 1850 1850 1870 AOSTIGAAGATITITITI 1843 AOSTIGAAGAAGAAGAAGAAGAAGAAGAAGAAGAAGAAGAAGAA
S288c long SKQ2n long	AAAAAAACCCOMAAAACATTAAACCOMAAACATTAAAACATTAATTAATTAATTAATTAATTAATT

Figure 96

EcoRI <u>IR'</u> mADHI Ampr 🖄 E_{coRI} GS Linker Axokine Fusion Leader Axoki FLP 'IR 14623 bps PRB1p NotI LEU2 R REP2 EcoRV EcoRL REF1 Ncol HindIII

EcoRI EcoRI Hind IIIEcoRI Axokine $pDB2617 \ {\tt GS \ Linker}$ Fusion Leader rHA mADH1t PRB1p 6787 bps Smal Nod Sm Nod SphI ori B AmpR Ndel

This Page is Inserted by IFW Indexing and Scanning Operations and is not part of the Official Record

BEST AVAILABLE IMAGES

Defective images within this document are accurate representations of the original documents submitted by the applicant.

Defects in the images include but are not limited to the items checked:

| BLACK BORDERS
| IMAGE CUT OFF AT TOP, BOTTOM OR SIDES
| FADED TEXT OR DRAWING
| BLURRED OR ILLEGIBLE TEXT OR DRAWING
| SKEWED/SLANTED IMAGES
| COLOR OR BLACK AND WHITE PHOTOGRAPHS
| GRAY SCALE DOCUMENTS
| LINES OR MARKS ON ORIGINAL DOCUMENT
| REFERENCE(S) OR EXHIBIT(S) SUBMITTED ARE POOR QUALITY

IMAGES ARE BEST AVAILABLE COPY.

☐ OTHER:

As rescanning these documents will not correct the image problems checked, please do not report these problems to the IFW Image Problem Mailbox.